

Multi-modal Molecular Imaging

TECHNOLOGY REVIEW CRITERIA FOR EURO-BIOIMAGING NODE

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This document describes the resources, which are either required or desirable to enable user access to integrated Multi-modal Molecular Imaging Technologies in Euro-BioImaging Nodes.

At the application date of the Expression of Interest to become a Euro-BioImaging Node, resources described here can either be already provided by the applying technology provider, or planned to be built up as a part of Euro-BioImaging Node application. In order to submit a successful application, each Node applicant is invited to provide as many resources listed here as possible. However, applications by technology providers who can only offer a selection of resources will also be considered.

All criteria listed here are defined as High Priority/Medium Priority for each technology individually in the Table 1.

In addition to the individual resources listed here, the Node should also have available support to handle the often complex administrative matters associated, in particular, with probes/contrast agents, animal facilities, cell culture, microscopy and biobanking.

In the use of multi-modal molecular imaging access in the framework of Euro-BioImaging, one expects to have considerable diversity between users, depending on their expertise and availability of certain technology in their home institution. Thus the future Node should have capacity to provide a broad range of support with project planning, experiment preparation, data acquisition & storage, data processing and analysis and training. Experienced staff to support users in all these activities and through all steps of the research project with the offered imaging modalities will be necessary. This mandatory comprehensive support will ensure that the facility and all its resources are utilized in the best possible way.

A Multi-modal Molecular Imaging Node provides excellence by the integration of multiple Imaging Technologies (Table 1). The Node may be single-sited or it may be multi-sited (see general eligibility criteria). The Node lists the procedures offered to the users outlining the ones the Node claims its excellent uniqueness. The Multi-modal Molecular Imaging Node can include one or more of the Flagship technologies that further strengthen and characterizes the Node.

The infrastructure must be able to support users of all levels of a Molecular Imaging experiment. Support should include: guidance on methodological set up, experiment preparation for offered technologies, image acquisition, data management, analysis and (technical) interpretation.

The feasibility and scientific value of the project should be evaluated and a detailed project plan agreed prior to user access. It is essential to have in place a project assessment and planning process that includes input from experienced technical and scientific staff. These staff should have the time and resources to contribute to this process. The process should include sign off of the agreed project plan by the user, scientific contact and where appropriate facility manager.

Staff at the infrastructure should be capable of advising users on the most appropriate choice among the portfolio of imaging modalities and validation experiments to deliver the research objectives for all project types that a Multi-modal Node will accept. In particular, Node Staff should help decide which imaging modalities they offer are best-suited for a particular experiment or sample type or help the user to test different modalities in a comparative manner at the beginning of the project.

Staff should also be able to maintain the different devices, guide measurements and help in interpreting data recorded across the range of imaging modalities offered. Tools for performing these analyses should be installed at the Node or be easily available from on-line resources.

As the duration of projects may vary (from ½ day to 1 year or more) nodes should be able to facilitate repeated visits by the users to the infrastructure at different stages of the project.

Multi-modal Molecular Imaging deals with the “in vivo” visualization, characterization and measurement of biological processes at the molecular, cellular and tissue levels by combining several tools and techniques with complementary characteristics in terms of sensitivity, specificity, temporal and spatial resolution. The imaging techniques include PET/SPECT, MRS/MRI, optical imaging, ultrasound, CT and others to enable insights into anatomical, functional and molecular processes in an integrative fashion, most often in combination with applied specific imaging agents. Molecular Imaging agents can be endogenous molecules or exogenous probes that use nuclear, magnetic, optical or other measures to generate image contrast. Quantification of the regional distribution of the image contrast is a central feature in multi-modal molecular imaging experiments and requires specific and standardized protocols for probe administration, image acquisition, processing, co-registration and analysis. In vivo Multi-modal Molecular Imaging results are validated by established in vitro molecular, genetic and histological tests. Multi-modal Molecular Imaging is interdisciplinary as it involves skills from general fields, including physics, chemistry, biology, imaging technology, medicine.

Multi-modal molecular imaging can tackle highly diverse scientific questions including among others: (i) development and test/validation of a novel imaging probe on state-of-art Imaging technology; (ii) test/validation of a new animal model with state-of-art probes/Imaging technology; (iii) monitor the therapeutic effects of a new drug using state-of-art probes/Imaging technology; (iv) compare/validate a new development in imaging technology with state-of-art imaging/models technologies; (v) compare/validate new developments in Image analysis with state-of-art imaging/models technologies both in preclinical and clinical settings. Thus, taking into account the broad application field and the interdisciplinary nature of multi-modal molecular imaging, it appears clear that a Multi-modal Molecular Imaging Node has to be implemented on an existing large Center or a consortium of highly qualified, complementary centers able to provide the wide scientific bases in terms of expertise and available instrumentation to tackle a wide-spread range of Multi-modal Molecular Imaging studies.

A Multi-modal Molecular Imaging Node should provide the following expertise or resources:

- 1) A portfolio of molecular imaging technologies ((micro)PET/SPECT, (micro)MRI/MRS, OI, (micro)US, (micro)CT, hybrid techniques) together with skilled personnel to maintain and operate the instruments on the highest level of scientific excellence.
- 2) Chemistry/radiochemistry for analytical/physico-chemical characterization and/or production of the imaging probes, together with the ability to store and distribute these probes.
- 3) Facilities for image validation are necessary for all access user projects and should range from simple sample staining over immunohistochemistry to autoradiography.

- 4) A wide variety of molecular probes such as magnetic resonance, nuclear, optical (bioluminescent, fluorescent, combined) and ultrasound imaging probes as well as biological reporters should be available at the facility, either through own production or commercially acquired. Since the imaging probes are key to enable molecular imaging, the infrastructure should offer a clear guidance on the specific probes to be used in order to fully exploit the potential of the selected imaging techniques.
- 5) Skilled staff to advise users on the most appropriate technology(ies), among their portfolio of imaging modalities, to deliver the research objectives for all project types that a Multi-modal Molecular Imaging Node will accept.
- 6) Competence, both scientific and technological, in application development
- 7) Expertise in image acquisition, processing, co-registration and analysis, either by commercial or in house built software, together with the experience to customize standard protocols to the specific user needs.
- 8) High level of integration among the available imaging platforms and between the imaging platforms and the additional infrastructure/resources.

To attain the high standards required in the Euro-Biolmaging Infrastructure, the application for a Multi-modal Molecular Imaging Node should provide sufficient information concerning the following items:

- i. The applicant will provide a detailed description of all the resources, which are considered required or desirable to enable user access to the Multi-modal Molecular Imaging Technology Node. This section of the application include access to a probe repository, to the analytical tools for physico-chemical characterization of the imaging reporters, to the characteristics of the available cell culture facilities and optical/fluorescent and electron microscopies, immunohistochemistry and FACS lab, to the facilities for image validation and for handling and preparation of small animals and the availability of specific animal models that can be made available to users.
- ii. As far as concern the experiments with animals, they have to be approved by the local (national institution) regulatory bodies and performed by personnel trained and skilled in laboratory animal anaesthesia and surgical support. Regulatory approvals need to be handled by the Node, prior to start the user access.
- iii. Transport and shipping: The animal facility should be staffed by appropriately trained personnel who have the capacity to plan for and deal with incoming animal models from, and their return to, international locations. All such processes will be carried out with close adherence to the local regulations at Node concerning animal experiments.
- iv. Facilities for the handling and preparation of model organisms are often necessary for users to culture and propagate specific model organisms required for experiments. The biobanking facilities should be located within easy working access and the same building as the imaging facility.
- v. Image processing and analysis workstations are necessary for most users particularly those who are accessing a Node for more than a few days. Nodes should have the

capacity to offer a basic workstation to all users accessing their facility, and where necessary, high-powered workstations with sufficient processing, memory and storage capacity to enable users to efficiently achieve their experimental aims.

- vi. Data storage is necessary for most users during access. Nodes should have the capacity to offer server space to users for storage of images and results. Data storage requirements vary greatly depending on the imaging technique used, but in general, capacity to store several tens to hundreds of Gigabytes is routine, and in certain cases, larger capacities will be necessary. In general, sufficient capacity to store both original and processed datasets from several users will be necessary.
- vii. Accommodation may be required by some users, particularly those who have travelled internationally to access a facility. Where a node can offer accommodation on site, this should be made clear to the user during the pre-visit preparation phase. If no accommodation is available on site, the Node should have the capacity to offer assistance in finding affordable accommodation.
- viii. Nodes should offer the capacity for planning on-site experiments with the applicant prior to physical access by the user. Assistance should include guidance on methodological set up required to obtain appropriate images, including guidance on the technology requirements for the preparation of samples, provision/procurement of materials required for image acquisition (appropriate stains, mounts etc). For some technologies more detailed project planning should be provided.
- ix. Nodes should offer a general induction or training programme for all visiting researchers. The induction should include documented safety and QM procedures for use of the technology and the supporting infrastructure to be accessed by the user.
- x. Nodes should have the capacity to support user access and provide expert support for operation of the imaging technologies being accessed. Facilities should offer documented procedures and expert assistance for operation of the technology and image acquisition. All staff offering support should be fully trained in the operation of the instrument.
- xi. Nodes should have the capacity to support users in image processing, co-registration and interpreting results. Documented guidance and expert advice on image processing, co-registration and analysis using offered technologies are essential.
- xii. To ensure that users achieve the objective of the requested access, thorough project planning by the Node staff will be required. Planning should also include safety and regulatory considerations, e.g. having facilities to rapidly obtain permissions for hosting/handling different cell lines etc.
- xiii. Some user projects could last several months and sometimes even beyond one year. This may require repeated visits of the users to the infrastructure at different stages of the project or for multiple iterations as users gain experience and redesign or optimise their experiments. The feasibility of longer term projects needs to be regularly reviewed, particularly during early stages, and projects could be refined or postponed until required preparatory work has been carried out or gaps in user training has been filled by Euro-BioImaging measures, as necessary. It is therefore essential to have in place a project management planning procedure and experienced staff able to over-see the project through all stages to support users.
- xiv. Nodes need to be able to support multiple users over extended periods and need dedicated flexible staff to support projects with diverse aims. Node staff needs to be

knowledgeable about the biological applications as well as their range of imaging techniques in order to be able to judge the capabilities and commitment of potential users.

- xv. With open access, the application of new instruments to new applications may be common and there could be a difficult learning curve for users as well as node staff. Nodes need to be able to support users over extended periods and to have appropriate staff, who have the time and resources to learn new skills or knowledge for specific projects. Staff will not be leading the user projects, however, and so must get appropriate recognition and career development in these support roles that will take up much of their time.
- xvi. A node should provide a friendly and expert infrastructure with specially trained and experienced staff who help to run the experiments, help with the interpretation of the acquired data and who host and train its users and teach them to use the facility in the best possible way. This comprehensive support is a mandatory quality control in order to ensure that data is recorded under optimal technical conditions.

Table 1: Technology Review Criteria for Multi-modal Molecular Imaging Node

Facility / Training		Priority Level	
		High	Medium
1.	(micro)PET/SPECT Scanner	X	
2.	(micro)MRI/MRS Scanner	X	
3.	Optical Imaging	X	
4.	(micro)CT Scanner		X
5.	(micro)US Scanner		X
6.	Chemistry Lab.	X	
7.	Radiochemistry Lab.	X	
8.	Cell Culture / Microscopy / Image Validation	X	
9.	Electron Microscopy		X
10.	Biobanking		X
11.	Repository of molecular probes	X	
12..	Workstations / ICT Access / Data Storage	X	
13.	Accommodation		X

14.	General Training Courses		X
15.	Methodological Set-up	X	
16.	Technical Assistance to prepare experiments and run instrument(s)	X	
17.	Image Processing and Analysis	X	
18.	Project Planning and Management	X	
19.	High Level of infrastructure Integration	X	